MCM team update: ADH6

We continue our work on characterizing lung cancer biomarkers identified in the MCM1 project. This update focuses on ADH6, a gene associated with smoking status and lung cancer prognosis.

Background

Recognizing patterns in cancer patients can have many benefits, such as making it possible to detect signs of cancer in other patients and personalizing each patient's treatment to fit their genetic profile. The Mapping Cancer Markers project analyzes databases with millions of data points collected from patients with cancers and sarcomas to find such diagnostic, prognostic and predictive signatures.

Since November 2013, World Community Grid volunteers have donated over 820,800 CPU/years to the project, helping analyze research data on cancers and sarcomas at a significantly faster pace and more thoroughly than otherwise possible. We are immensely grateful for the volunteers who continue to donate to this project.

We continue our work on common lung cancer biomarkers. VAMP1, FARP1, and GSDMB were discussed in our March, April, and July updates. Here, we introduce information on ADH6.

ADH6 Research

Alcohol dehydrogenase 6 (ADH6) is a member of the zinc-containing alcohol dehydrogenase family, a group of enzymes that enable the conversion of alcohols to aldehydes (UniProt). ADH6 is a separate type of alcohol dehydrogenase, and is not as well documented as other members of its family. It has only a predicted structure (Figure 1), and only 27 interacting partners (Figure 2), but one of those being a well-known and important lung cancer protein, KRAS.

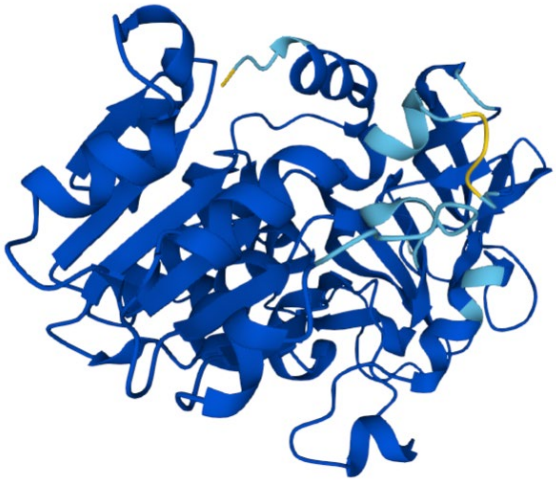

Figure 1. Protein structure of ADH6 (UniProt).

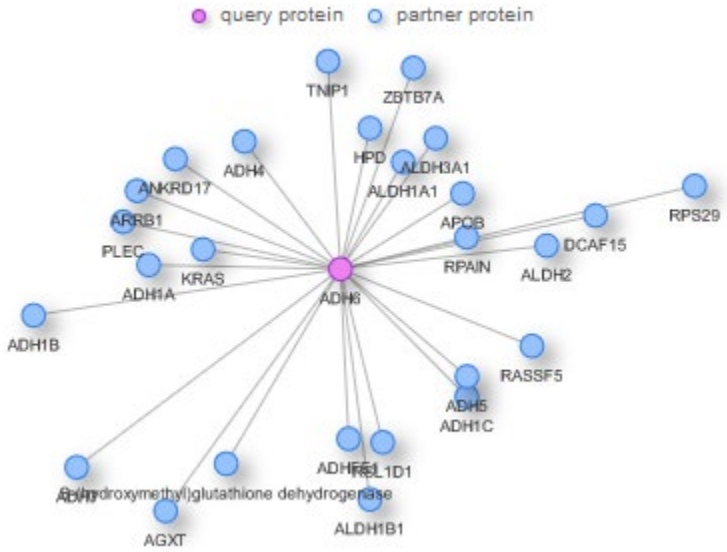

Figure 2. Physical protein partners of ADH6 (IID)

As shown in Figure 3, ADH6 has a significantly lower expression in lung cancer cells compared to normal tissue. Studies have identified ADH6 as a prognostic marker of lung adenocarcinoma, the most common type of lung cancer [1]. Additionally, ADH6 expression has been found to be associated with smoking status [2,3]. Other studies have found that expression levels of ADH6 are also associated with survival rate in patients with liver cancer [4,5].

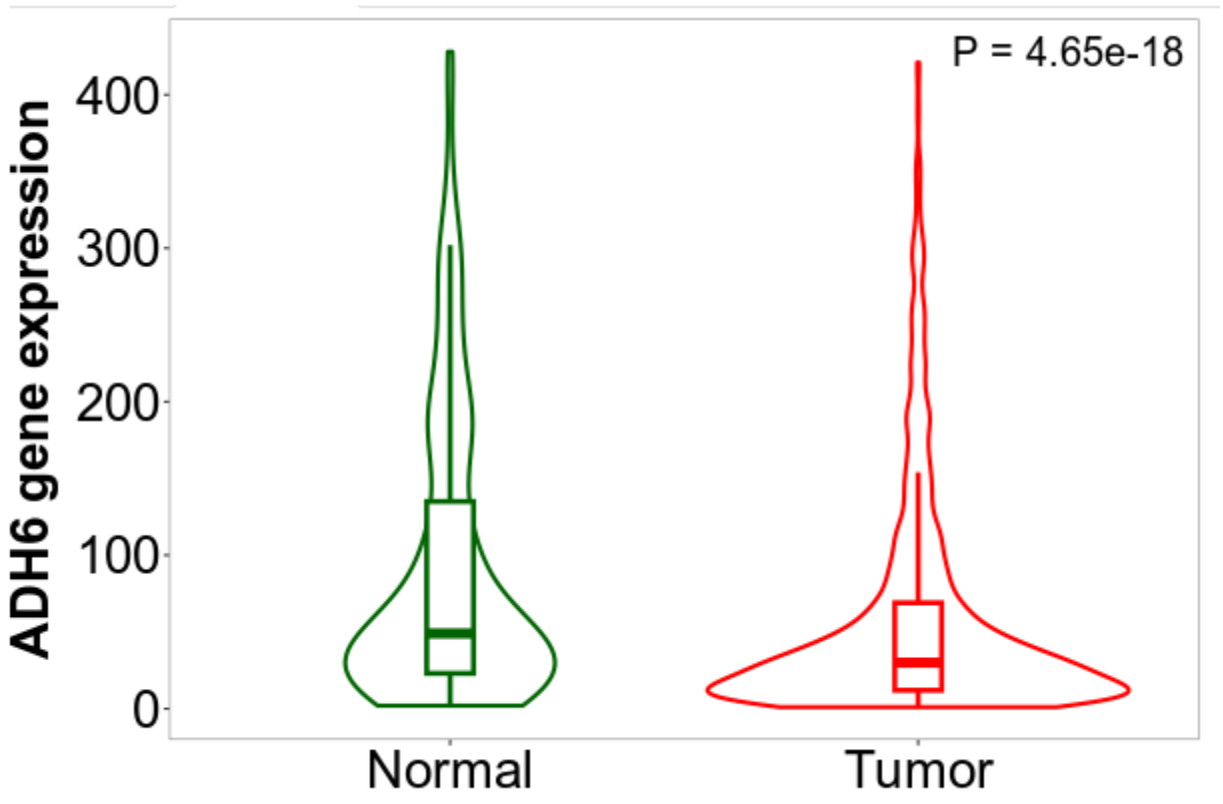

Figure 3. Expression of ADH6 in normal and cancer tissues in the human lung (TNMPlot).

We and others have shown that many cancer genes are aberrantly re-activated components of processes normally active during organ and organism development. Proteins and processes related to brain development are especially important since lung to brain metastasis is identified in 25% of lung cancer patients at diagnosis and there is a lifetime risk of 50% developing brain metastasis from lung cancer. ADH6 shows strong overexpression in the choroid plexus during development (Figure 4).

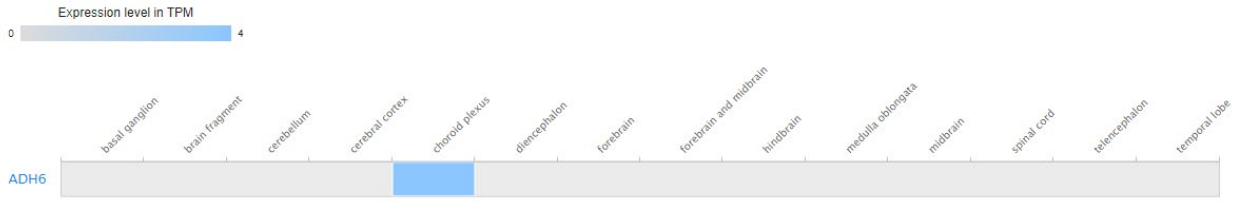

Figure 4. ADH6 overexpression in the developing brain (Expression Atlas).

While we study ADH6 due to lung cancer involvement, there is evidence this gene plays a role in many other cancers and conditions (Figure 5).

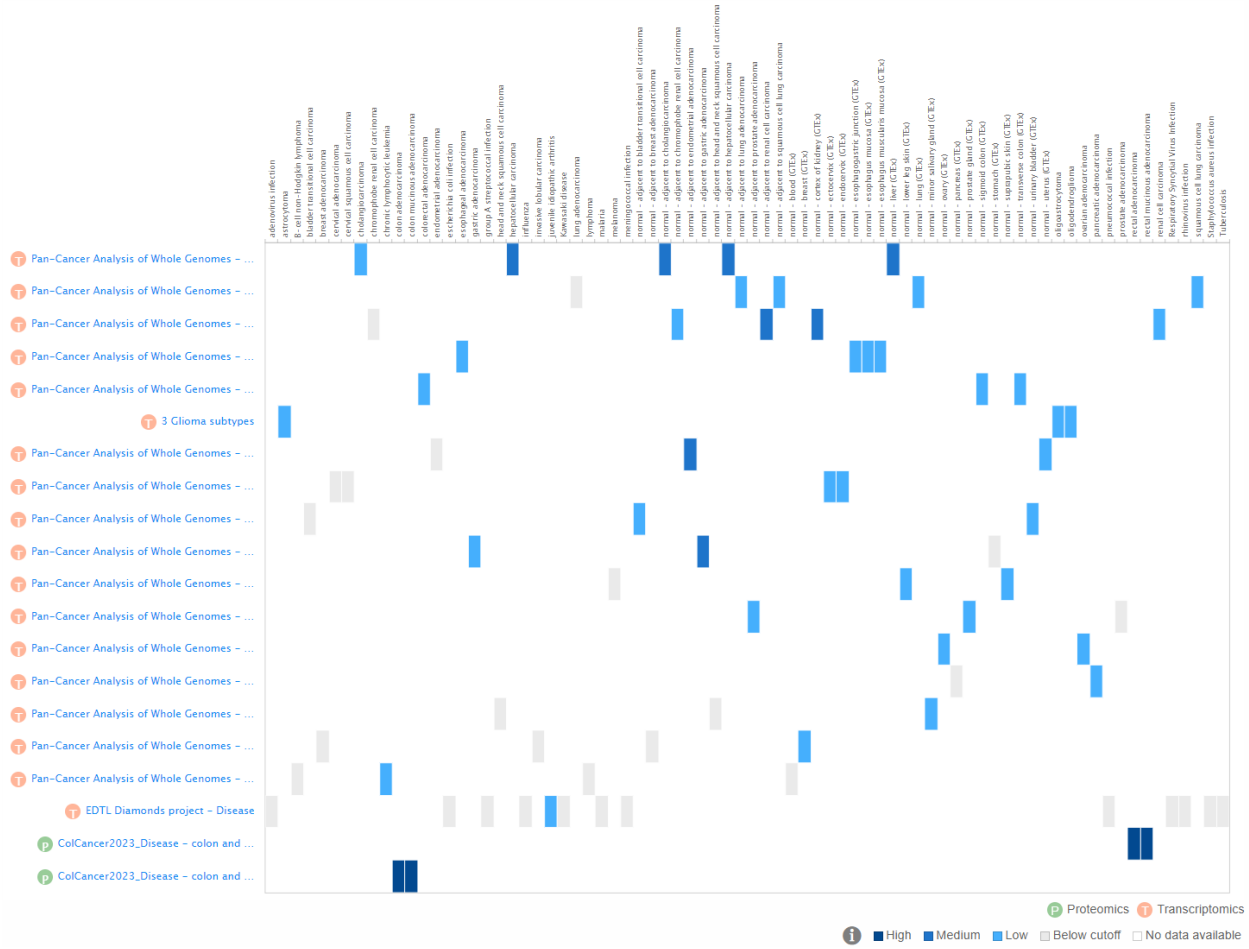

Figure 5. ADH6 overexpression across multiple cancers and diseases (Expression Atlas).

If you have any comments or questions, please leave them in this thread for us to answer. Thank you for your support, patience and understanding.

WCG team (https://www.cs.toronto.edu/~juris/jlab/mcm.html)

References:

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